PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P031668WO: CJM		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB 03/04295	01.09.2003	30.08.2002

International Patent Classification (IPC) or both national classification and IPC
C12N15/31

Applicant
CHIRON SRL et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.03.2004	08.09.2004

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Mandl, B

Telephone No. +49 89 2399-8434

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/04295

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-39 as originally filed

Claims, Numbers

1-15 as originally filed

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 14, with regard to industrial applicability

   because:

   ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-15
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-13,15
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 14 relates to subject-matter considered by this Authority to be covered by the provisions of **Rule 67.1(iv) PCT**. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (**Article 34(4)(a)(i) PCT**).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 9517211 (BIOCINE S.P.A.); 29 June 1995
D2: WO 02 079242 A (CHIRON SPA); 10 October 2002

1) Article 33(2) PCT

i) Document **D1** is regarded as being the closest prior art to the subject-matter of claims 1,5 and 8-15 because it discloses detoxified mutants of bacterial ADP-ribosylating toxin.

ii) The subject-matter of claims 1,5 and 8-15 relates to detoxified mutants of the ADP-ribosylating toxin of *Neisseria meningiditis*. *Neisseria meningiditis* toxin has not been referred to in D1.

iii) The subject-matter of claims 1,5 and 8-15 is therefore new.

2) Article 33(3) PCT

i) The problem to be solved by the present invention may be regarded as the detoxification of ADP-ribosylating toxin of *Neisseria meningiditis* by introduction of mutations.

ii) The solution to this problem proposed in claims 1,5 and 8-15 of the present ap-

plication is considered as involving an inventive step (**Article 33(3) PCT**) because it could not be derived from the prior art, where the toxin has to be mutated in order to solve the problem posed.

3) Dependent claims

Claims 2-4,6 and 7 are dependent on claims 1 and 5 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4) Priority

i) The validity of the priority has not been checked.

ii) However, above comments with regard to novelty and inventive step only apply if the priority can be validly claimed.

iii) If the priority of the present application turns out to be invalid, the filing date will become the effective date. Consequently, document D2 will form part of the prior art and anticipate the novelty of claims 1-15 for the following reason:

iv) **D1** discloses mutant *Neisseria meningitidis* ADP-ribosylating enzyme wherein the mutant has a substitution at one or more of amino acids Glu-109, Glu-111 or Glu-120. The mutant also has reduced or eliminated ADP-ribosyltransferase and/or NAD-glycohydrolase activity relative to the wild-type enzyme which corresponds to SEQ ID NO: 1 of the present application. In one specific embodiment, the one or more of amino acids Glu-109, Glu-111 or Glu-120 are substituted with Asp (D1: page 2, lines 7-22, SEQ ID NOs: 12, 14 and 16 and Table 1). D1 claims uses of this mutant as immunogenic compositions and adjuvant.